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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/842,337	04/25/2001	Charles Jack Fisher	X-12449A	7545

25885 7590 12/15/2003

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EXAMINER	
WEBER, JON P	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 12/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/842,337	FISHER ET AL.	
	Examiner	Art Unit	
	Jon P Weber, Ph.D.	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,11 and 12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,11 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *10/16/03* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 16 October 2003 has been entered. Claims 1 and 11-12 have now been presented for examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 1 and 11-12 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is argued that the disclosure suggests treating viral hemorrhagic fever and provides relevant dose ranges. It is urged that examiner's general disbelief is inadequate to support a rejection. It is urged that the zymogen can be converted to aPC in vivo similarly to a prodrug by activation by limited proteolysis by thrombin. Viral hemorrhagic fever is asserted to be a hypercoagulable state and that during such state, there is increased thrombin which would lead to increased activation of the zymogen. In support of this argument, Takazoe et al., Granger et al.,

Mesters et al. (1996), Mesters et al. (2000) and de Kleijn et al. are cited that elevated thrombin correlates with increased levels of aPC in various disease states including hypercoagulable state. It is also argued that zymogen has been administered in studies reported by Gerson et al., Rivard et al., and Rintala et al. The EMEA document supporting use of zymogen for purpura fulminans and coumarin-induced skin necrosis was not available for consideration.

It is argued that, "There must be reason to doubt the objective truth of the statements contained within the specification, which includes the claims, and an explanation as to why the Examiner does not believe the statements which the Applicants have set forth in the specification. See M.P.E.P. 2164.04."

The instant disclosure is prophetic and therefore speculative in nature. Speculation is not objective truth. Objective truth is based upon factual evidence. Since there are no working examples, one must consider the state of the art. Examiner has established with Bang et al. that the conversion of zymogen to aPC is slow process, so much so, that it is not clear that therapeutic levels of aPC can be reached for any disease state, let alone the specific viral hemorrhagic fever treatment instantly claimed.

Consider Takazoe et al., Granger et al., Mesters et al. (1996), Mesters et al. (2000) and de Kleijn et al. provided in support. These studies show that elevated thrombin in various disease states causes a statistically significant increase in aPC. This is consistent with the mechanism of activation of the zymogen by thrombin. However, this is activation of endogenous zymogen and does not clearly indicate that administration of exogenous zymogen to treat viral hemorrhagic fever will increase aPC above and beyond that level or that the level of aPC achieved will be

therapeutic for viral hemorrhagic fever. Further the language "statistically significant" suggests that the level of increase was just detectable.

Treatment with zymogen is not shown by any of Gerson et al., Rivard et al., and Rintala et al. These studies report use of a commercially available aPC concentrate, not the zymogen. Their relevance to zymogen administration is not clear. The relevance of the EMEA document to the use of zymogen to treat viral hemorrhagic fever is also not clear. This document was not available for consideration but at best can be assumed to establish safety and efficacy for treatment of the specific diseases indicated and not treatment of other disease such as viral hemorrhagic fever. It is relevant to note that this publication is after the instant filing date. Further, the EMEA www site was searched but a document showing any treatment with protein C zymogen was not found. Instead a document was found describing a plasma derived activated protein C concentrate (CEPROTIN) produced by Baxter AG for treatment of purpura fulminans and coumarin-induced skin necrosis (The same document allegedly provided in the Disclosure Statement?).

To quote from page 27 of this document:

> Since the safety/efficacy profile of this product has not been fully established yet, its use is deemed relatively safe and effective only in the severe clinical conditions for which it is indicated.

It is thought that this material is similar to or identical to that used by Gerson et al., Rivard et al., and Rintala et al. in their studies. Accordingly, there is no art of record showing the administration of zymogen for the treatment of any disease state, only aPC concentrates.

Applicant's arguments filed 16 October 2003 have been fully considered but they are not persuasive. The rejection under 35 U.S.C. 112, first paragraph is adhered to for the reasons of record and the additional reasons above.

No claims are allowed.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon P Weber, Ph.D. whose telephone number is 703-308-4015. The examiner can normally be reached on daily, off 1st Fri, 9/5/4.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 703-308-4743. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

My new Office room number will be Rem-03A45 and my new Office phone number will be 571-272-0925 after 15 January 2004.

Jon P Weber, Ph.D.
Primary Examiner
Art Unit 1651

JPW
10 December 2003